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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/125,122	01/04/1999	GIULIO TARRO	A31920-PCT-U	7447

21003 7590 12/20/2001

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EXAMINER
BUNNER, BRIDGET E

ART UNIT	PAPER NUMBER
1647	21

DATE MAILED: 12/20/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/125,122	TARRO ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,9,11,13,15,17 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,9,11,13,15,17 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

The Request for Continued Examination (RCE) filed on 12 October 2001 (Paper No. 19) under 37 CFR 1.114 based on parent Application No. 09/125,122 is acceptable and an RCE has been established. An action on the RCE follows.

Status of Application, Amendments and/or Claims

The amendment of 12 October 2001 (Paper No. 20) has been entered in full. Claim 7 is amended and claim 19 is cancelled.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 7, 9, 11, 13, 15, 17, and 20 are pending and are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The rejection of originally filed claims 7, 9, 11, 13, 15, 17, 19, and 20 under 35 U.S.C. § 103(a) in the previous Office Action (Paper No. 18, 14 May 2001) is *withdrawn* in view of Applicant's arguments and amended claim (Paper No. 20, 12 October 2001). Please see rejections under 35 U.S.C. § 102(b) and 35 U.S.C. § 103(a).

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "METHOD OF TREATING VIRAL HEPATITIS C BY ADMINISTRATION OF LIQUID HUMAN α-INTERFERON".

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 7, 9, 11, 13, 15, 17, and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. The term "natural" in claims 7, 9, 11, 13, 15, 17, and 20 is a relative term which renders the claim indefinite. The term "natural" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It cannot be determined if "natural" is referring to a product of nature or a product by the hand of man. (Please note that this issue could be overcome by removing the word "natural" from claims 7 and 20.)

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 20 is rejected under 35 U.S.C. 102(b) as being anticipated by Cummins et al. (WO 88/03411).

Cummins et al. teaches a pharmaceutical agent, human alpha interferon, and its process of preparation (pg 13-16). Cummins et al. also teaches that human α-interferon as a liquid formulation is administered through the peroral route at a daily dosage of 0.01 to about 5 IU per

pound (pg 27, 29-31; claim 1). Therefore, for typical patients weighing from about 100 to 225 pounds, the preferred dosages are thus on the order of 5-1,125 IU α-interferon per day. Additionally, the recitation of "packaging material/label" in claim 20 fails to distinguish the claims from prior art because written material is not protected under patent law. Also, the written material is tantamount to an intended use, which is not given patentable weight.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 7, 11, 13, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Di Bisceglie et al. (New England J Med 321: 1506-1510, 1989) in view of either one of Cummins (U.S. Patent No. 5,824,300) or Cummins et al. (WO 88/03411).

Di Bisceglie et al. teaches daily subcutaneous administration of human α-interferon to subjects having type C viral hepatitis (abstract; pg 1506, col 2).

Di Bisceglie et al. does not teach administration of an oral liquid formulation of human α-interferon at a daily dosage of between 100 and 500 IU. Di Bisceglie et al. also does not teach that the human α-interferon is obtained from lymphocyte cells.

Each of the Cummins references describes aqueous formulations of human α-interferon which are suitable for use in the therapeutic methods it describes and claims (*See* '300 at col. 3; '411 at pages 5-6; and the claims of each). Such methods call for delivery to the oropharyngeal mucosae of α-interferon in solution at dosages preferably ranging from about 0.5 to 1.5 IU per pound per day ('300 at claim 3; '411 at claim 1). For typical patients weighing from about 100 to 225 pounds (*ca.* 45-100 kg), the preferred dosages are thus on the order of 50 to 340 IU α-interferon per day. Among the preferred sources of α-interferon are buffy coat leukocytes ('300, col. 3, lines 25-35; '411, page 4, lines 2-6). Each of the references teaches that the human α-interferon may be administered once daily or in divided doses ('300 at col. 5, lines 56-61; '411 at the paragraph bridging pages 11-12). Furthermore, Cummins teaches administration of an oral liquid formulation of human α-interferon to patients twice daily at a dosage of 0.7 IU per pound ('300 at col. 12; '411 at page 27). Therefore, for typical patients weighing from about 100 pounds to 225 pounds, the preferred dosages are thus on order of 140 to 315 IU of α-interferon per day. The human α-interferon is administered in a buffered solution having a concentration such that a single dosage could be administered in a volume of about 1 to about 20 milliliters of liquid ('300 at col. 12; '411 at page 27). Other exemplary formulations described by Cummins

contain 1-1500 IU of α-interferon in a dosage volume of one tablespoon (15 ml), or 0.07-100 IU ml^{-1} of cough syrup ('300 at col. 14, lines 1-5; '411 at page 31, first full paragraph).

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a liquid formulation containing 1-1500 IU of human leukocyte α-interferon in a convenient single-dose delivery volume for oral administration as taught by Cummins to treat a subject having type C viral hepatitis as taught by Di Bisceglie et al. The person of ordinary skill in the art would have been motivated to make that modification because oral delivery of α-interferon (contact with the oral and pharyngeal mucosa) would achieve better results as compared to other forms of delivery, such as intramuscularly or intradermally. The person of ordinary skill in the art would have expected success because human α-interferon was already being administered to subjects with type C viral hepatitis at the time the invention was made. The intended uses recited in the instant claim impose no material or functional limitations on the formulations *per se* or the methods of making them and thus do not patentably define over the prior art formulations.[1] The claimed invention would have been *prima facie* obvious as a whole at the time it was made, especially in the absence of evidence to the contrary. The concentration range claimed by applicant overlaps the prior art range, and the prior art and the claimed formulations comprise the same active ingredients and are employed in the same manner, *i.e.*, oral delivery in a manner that promotes contact between the liquid α-interferon solution and the oropharyngeal mucosae.

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[1] It is however noted that each of the Cummins references teaches that its formulations are suitable, *inter alia*, for the treatment of viral and neoplastic diseases according to the methods it describes.

11. Claims 9 and 15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Di Bisceglie et al. and either one of Cummins '300 or '411 as applied to claims 7, 11, 13, and above, further in view of Ratajczak et al. (Arch. Immunol. Ther. Exp. 41: 237-40, 1993).

The relevant teachings of the Di Bisceglie et al. and Cummins references are as discussed above in connection with the rejections under § 103(a). Neither describes a formulation employing lymphoblastoid human α-interferon.

Ratajczak describes the use of lozenges containing 50 or 100 IU of human lymphoblastoid α-interferon for oropharyngeal delivery in the treatment of hepatitis B infections. *See* the title and page 239, col. 1, first paragraph.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare an aqueous formulation of human α-interferon according to Cummins '300 or '411, employing lymphoblastoid α-interferon as described by Ratajczak in place of the buffy coat leukocyte α-interferon noted particularly by Cummins, because Ratajczak evidences that lymphoblastoid interferon was readily available at the time of the invention and teaches that it is suitable for the treatment of an exemplary viral disease *via* delivery to the oropharyngeal mucosae. It consequently would have been obvious to the artisan that lymphoblastoid interferon would be the functional equivalent of the human α-interferon liquid preparations expressly described by Cummins in the '300 and '411 references for use in the treatment of subjects having type C viral hepatitis as described in Di Bisceglie et al. The claimed invention would have been *prima facie* obvious as a whole at the time it was made, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

Davis et al. New England J Med 321(22): 1501-1506, 1989.

Marcellin et al. Hepatology 13 : 393-397, 1991.

Main, J. J Hepatology (Suppl) 23(2): 32-36, 1995.

Toyoda et al. Am J Gastroenterol 89(9) : 1453-1457, 1994.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Elizabeth C Kemmerer

BEB
Art Unit 1647
December 6, 2001